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MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU,
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(54) Title: MATRIX METALLOPROTEINASE INHIBITORS

(57) Abstract: Compounds are provided that bind allosterically to the catalytic domain of MMP-13 and comprise a hydrophobic group, first and second hydrogen bond acceptors and at least one, and preferably both, of a third hydrogen bond acceptor and a second hydrophobic group. Cartesian coordinates for centroids of the above features are defined in the specification. When the ligand binds to MMP-13, the first, second and third (when present) hydrogen bond acceptors bond respectively with Thr245, Thr247 and Met 253, the first hydrophobic group locates within the S1' channel of MMP-13 and the second hydrophobic group (when present) is relatively open to solvent. The compounds specifically inhibit the matrix metalloproteinase-13 enzyme and thus are useful for treating diseases resulting from tissue breakdown, such as heart disease, multiple sclerosis, arthritis, atherosclerosis, and osteoporosis.

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INTERNATIONAL SEARCH REPORT

International application No. -

PCT/IB02/00447

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : A61K 31/16, 31/36, 31/41, 31/44, 31/505, 31/517, 31/519, 31/54; A61P 19/00; C07C 233/00; C07D 213/02, 239/02, 239/72, 285/14, 285/22, 317/44, 401/02, 417/02, 495/02
US CL : 514/223.2, 257, 259.2, 260.1, 264.1, 266.3, 274, 332, 361, 466, 616; 544/12, 250, 251, 278, 279, 284, 285,

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : Please See Continuation Sheet

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAS ONLINE (search terms: MMP-13)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	MOY et al., High-Resolution Solution Structures of the Catalytic Fragment of Human Collagenase-3 (MMP-13) Complexed with a Hydroxamic Acid Inhibitor, Journal of Molecular Biology, 22 September 2000, Vol. 302, No. 3, pages 671-689.	1-45
A	CHEN et al., Structure-Based Design of a Novel, Potent, and Selective Inhibitor for MMP-13 Utilizing NMR Spectroscopy and Computer-Aided Molecular Design, Journal of the American Chemical Society, 11 October 2000, Vol. 122, No. 40, pages 9648-9654.	1-45
A	LOVEJOY et al., Crystal Structures of MMP-1 and -13 Reveal the Structural Basis for Selectivity of Collagenase Inhibitors, Nature Structural Biology, March 1999, Vol. 6, No. 3, pages 217-221.	1-45



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"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

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Continuation of B. FIELDS SEARCHED Item 1:

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